

PATENT  
4367-0106PUS1

## IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant: HAYASHI et al. Conf.: UNASSIGNED  
Appl. No.: 10/517,599 Group: UNASSIGNED  
Filed: December 13, 2004 Examiner: UNASSIGNED  
For: ALKYNYPURINE COMPOUNDS AND PRODUCTION  
METHODS THEREOF

LETTER

APR 28 2005

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Subsequent to the filing of the above-identified application on December 13, 2004, attached hereto is an English translation of the International Preliminary Examination Report (Form PCT/IPEA/409) that should be made of record in the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or to credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH &amp; BIRCH, LLP

By

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## PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT  
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 09549		<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEAA416)	
International application No. PCT/JP 03/07317	International filing date (day/month/year) 10.06.2003	Priority date (day/month/year) 14.06.2002	
International Patent Classification (IPC) or both national classification and IPC C07D473/00			
Applicant SUMIKA FINE CHEMICALS CO., LTD. et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand  18.11.2003		Date of completion of this report  13.08.2004	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer  Goss, I  Telephone No. +49 89 2399-8292	



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/JP 03/07317

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

- D1: EP-A-0 488 336
- D2: ADAH S A ET AL: 'Triflic Enolates In the Palladium-Mediated Synthesis of Complex Ethynyl Adenosines' TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 36, no. 36, 4 September 1995 (1995-09-04), pages 6371-6372, XP004027233
- D3: NAIR V ET AL: 'STRATEGICALLY FUNCTIONALIZED ADENOSINES: AGONISTS FOR ADENOSINE RECEPTORS' NUCLEOSIDES & NUCLEOTIDES, MARCEL DEKKER, INC, US, vol. 14, no. 3-5, 1995, pages 537-539, XP009017441
- D4: HOCEK M ET AL: 'COVALENT ANALOGUES OF DNA BASE-PAIRS AND TRIPLETS. PART 2: SYNTHESIS AND CYTOSTATIC ACTIVITY OF BIS(PURIN-6-YL)ACETYLENES, -DIACETYLENES AND RELATED COMPOUNDS' BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 12, no. 7, 2002, pages 1055-1058, XP009017440
- D5: HOCEK M ET AL: 'COVALENT ANALOGUES OF DNA BASE-PAIRS AND TRIPLETS V+. SYNTHESIS OF PURINE-PURINE AND PURINE-PYRIMIDINE CONJUGATES CONNECTED BY DIVERSE TYPES OF ACYCLIC CARBON LINKAGES' COLLECTION OF CZECHOSLOVAK CHEMICAL COMMUNICATIONS, ACADEMIC PRESS, LONDON, GB, vol. 67, no. 10, 2002, pages 1560-1578, XP009017464
- D6: MAGER P P: 'NEURAL NETWORK APPROACHES APPLIED TO SELECTIVE A2A ADENOSINE RECEPTOR AGONISTS' MEDICINAL CHEMISTRY RESEARCH, BIRKHAUSER, BOSTON, US, vol. 8, no. 6, 1998, pages 277-290, XP000952528
- D7: LEGRAVEREND M ET AL: 'Synthesis of C2 alkynylated purines, a new family of potent inhibitors of cyclin-dependent kinases' BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 8, no. 7, 7 April 1998 (1998-04-07), pages 793-798, XP004136967
- D8: CAMAIONI E ET AL: 'NEW SUBSTITUTED 9-ALKYLPURINES AS ADENOSINE RECEPTOR LIGANDS' BIOORGANIC & MEDICINAL CHEMISTRY, ELSEVIER SCIENCE LTD, GB, vol. 6, no. 5, 1998, pages 523-533, XP002926121

**INTERNATIONAL PRELIMINARY  
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International application No. PCT/JP 03/07317

- D9: MATSUDA A ET AL: 'Nucleosides and nucleotides. 103. 2-Alkyladenosines: a novel class of selective adenosine A2 receptor agonists with potent antihypertensive effects' JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 35, 1992, pages 241-252, XP002170995
- D10: BAKKESTUEN A K ET AL: '9-Benzylpurines with inhibitory activity against Mycobacterium tuberculosis' BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 10, no. 11, June 2000 (2000-06), pages 1207-1210, XP004200557
- D11: EP-A-1 054 012

**1. Novelty**

The subject-matter independently claimed in claims 1 and 5 for compounds of general formula I-1 as well as I-2 is not novel in view of the many novelty destroying documents cited in the search report. In this respect the applicant's attention is drawn to each single compound, example or figure as quoted in the search report wherein 2-, 6-, or 8-alkynylpurines have been described. Also the meaning of Z<sup>1</sup> and Z<sup>2</sup> (present nomenclature) being a sugar group, for example pentoses, attached at the 7- or 9-position of the purine nucleus is already known from the prior art. No further characterising structural element could have been identified.

By restoring novelty (if possible), the novelty rendering feature vis-à-vis the many compounds known from the prior art and also active in the same technical field, has to be clearly indicated.

**2. Inventive step**

As long as novelty cannot be recognized, a final opinion on inventive step cannot be given. As already anticipated under item 1., by restoring novelty, attention must be paid to define the technical contribution to the already many compounds known from the state of the art, all showing the same pharmacological profile (the aspect of unity of the invention must be carefully considered).

Therefore taking into account **the whole prior art available** an obviousness objection has to be raised, since the skilled person would have tried to provide further compounds expecting them to have the same qualitative activity as those known from D1 to D10.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/JP 03/07317

Consequently, at present it is not possible to first recognize

- a) whereon exactly an inventive step could be based, bearing in mind that the problem must have been to provide better compounds (i.e. with improved or unexpected properties) than those already known from the prior art.
- b) Further, the problem must be solved by all the compounds claimed re those of the relevant prior art.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/JP 03/07317

**I. Basis of the report**

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17):*

**Description, Pages**

1-53 as originally filed

**Claims, Numbers**

1-23 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/JP 03/07317**

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	
	No: Claims	1-23
Inventive step (IS)	Yes: Claims	
	No: Claims	1-23
Industrial applicability (IA)	Yes: Claims	1-23
	No: Claims	

**2. Citations and explanations**

**see separate sheet**